

BRANNAN (J.W.) & CHEESMAN (T.M.)

A STUDY
OF
TYPHUS FEVER

*CLINICAL, PATHOLOGICAL, AND
BACTERIOLOGICAL*

BY

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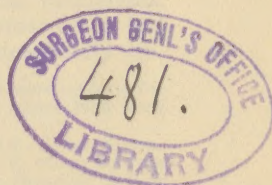
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A STUDY OF TYPHUS FEVER,¹

CLINICAL, PATHOLOGICAL, AND BACTERIOLOGICAL.

TYPHUS FEVER is, fortunately, a rare disease in this country, and the few epidemics of which we have record are all directly traceable to importation from Europe. The reports of Dr. R. Robertson, a surgeon in the English navy during the War of the Revolution, show that in 1776 the fever prevailed among the British and American sailors in the naval hospitals at New York and Newport, but it apparently never spread to the townspeople nor to the armies operating on shore. Nathan Smith, writing in 1824, states that he saw "typhous" fever as early as 1787, in New Hampshire; but it is evident from his description that it was typhoid fever, and not typhus fever as now recognized.

The first well-authenticated outbreak of the disease was in the year 1807, at Hartford, and two or three other points in New England. The fever was epidemic in Philadelphia in 1812, and again in 1836. It was in the latter year that Gerhard made the observations which have had a large share in establishing a correct idea of the disease. The first considerable epidemic in New York was in 1847, following the Irish famine of that year. In 1861 the disease was again introduced here by Irish immigrants, and did not finally disappear until three years had elapsed. Since that time it has been twice mildly epi-

¹ The clinical observations recorded in this paper were made in the wards of the Riverside Hospital, on North Brother Island, New York City.

The writers desire to express their thanks to Dr. Cyrus Edson, now Sanitary Superintendent of New York City, to whom they are indebted for the privilege of visiting the Riverside Hospital; and to Dr. F. R. Percival, late Resident Physician at the Hospital, who gave them most efficient aid in the wards of that institution.

To Professor T. Mitchell Prudden, Director of the Pathological Laboratory, College of Physicians and Surgeons, Columbia College, they wish to express their obligations for his advice and assistance, rendered during the pursuance of their histological and bacteriological researches in the laboratory.

demic in this city—in 1881, and again in February of the present year. In all these cases the fever was brought to this country by immigrants from regions where it is endemic. It is an interesting fact that the disease has never become endemic here, but has always disappeared when suitable hygienic measures have been brought to bear upon it. It is believed to be always present in Ireland, Russia, Poland, and Bohemia. This endemicity has been attributed to certain characteristics of the races in those countries, which serve to perpetuate the germ. But we have many thousands of those races here, and yet the disease never breaks out among them spontaneously, nor do they show an especial susceptibility to the imported contagion. In the recent epidemic, indeed, the mortality was much heavier among the Americans who acquired the disease than among the Russian Hebrews who brought it with them. The fact that typhus fever was not introduced into America until comparatively recent years has probably much to do with our exemption from its ravages. Had the immigrants of the last century been infected with the disease, it might well have obtained a firm foothold among us. But modern sanitation has taught us how to fight such diseases, and it now requires but a comparatively short time to get them under control, provided they are recognized before they have spread too widely.

A comparison between the epidemic of 1861 and that of February of this year will show what can be accomplished by intelligent and energetic hygienic measures. In 1861¹ the first case was that of a little girl, who was brought into a tenement-house in Mulberry Street, ten days before she became ill, from a ship which had had cases of typhus fever on board. Two weeks after her illness began, her aunt took the disease and died. In gradual succession nearly every family in the building took the fever. Becoming frightened, some of these families moved into other streets, formed the nucleus for the development of the disease in different localities, and it soon became a widespread epidemic. There was constant and unrestrained intercourse between the healthy and the sick. As a result of this lack of supervision and control the epidemic lasted for three years, and several thousand persons suffered from the fever. Let us contrast these figures with those of the recent epidemic.

On February 11th, Dr. Edson, Chief Inspector of Contagious Diseases, learned of the presence of 44 cases of typhus fever in this city. All these cases were among Russian Hebrews who had arrived in this port a few

¹ A. L. Loomis: Practical Medicine, p. 714.

days previously in the steamship *Massilia*. This emergency called for immediate action. As stated by Dr. Edson,¹ there are only two ways of fighting typhus fever. These are : 1, Isolation of the sick and those exposed to the contagion ; and 2, the destruction, or thorough disinfection, of all articles which may have come in contact with the sufferers. These measures were both carried out on this occasion, with the result that the disease was soon well under control. The sick persons, as well as all known to have been exposed to the contagion, were at once transferred to the Hospital for Contagious Diseases on North Brother Island. The 44 original cases had been found distributed in several lodging-houses filled with other Hebrews, and yet only 185 persons in all suffered from the fever.²

It is now generally admitted that typhus fever never arises spontaneously, but is always due to contagion from a previously infected individual. But there are certain conditions which favor greatly the spread of the specific poison. These conditions are overcrowding, filth, and destitution. Murchison, indeed, believed that such conditions of themselves were sufficient to generate the disease *ae novo*. David Hosack, also, as a result of his observation of the disease in New York, wrote, in 1820 : "Typhus is the product of confined human effluvia, the result of the filthy mode of living unavoidable among the poor." Such was the common opinion in the early part of this century among physicians both in Europe and in this country. Murchison cites many observations in support of his theory of spontaneous generation, but in the light of modern experience they carry no weight whatever.

The importance of early diagnosis has been alluded to above. Unfortunately, during the first two or three days there is but little to distinguish typhus from any other fever.

The onset is usually sudden. The patient has a distinct chill or sense of chilliness. This is followed by severe headache, and pains and aching in the back and limbs. A sense of extreme prostration is felt almost at once, and many patients take to their beds on the first day of their illness. This prostration is accompanied with loss of appetite, coated tongue and high fever. These symptoms are present within the first twenty-four hours, but are not of themselves sufficient to warrant a diagnosis of typhus fever. Perhaps at this early period

¹ North American Review, April, 1892.

² Since the preparation of this paper a few additional cases have been reported.

the abrupt rise of temperature, reaching sometimes 40.5° C. on the first day, and the great prostration, are the most noteworthy symptoms. The prostration increases as the disease advances, reaching its maximum on the tenth to the twelfth day. The fever presents no marked remissions during the first ten days, varying but little from 40.5° C. Then it defervesces more or less rapidly in cases ending in recovery, reaching normal figures on about the fourteenth day.

The typhus facies is usually referred to as characteristic of the disease, and it was very marked in most of the cases seen in the recent epidemic. On entering a ward containing perhaps twenty five beds, one was at once struck by the uniformity of expression of the occupants. This was probably partly due to the fact that they all belonged to the same race of peculiar people, at least in the beginning of the epidemic. But the same physiognomy was also noticeable when other nationalities were gradually introduced, taking the beds vacated by the Hebrews who had gone before. There was the same congested, dusky face. The conjunctivæ were injected, the eyelids and lips, as a rule, half-opened when the patient was lying undisturbed. The absence of any anxiety in the face was also marked. Not one of the patients with whom I came in contact expressed any concern as to the outcome of his own illness, though when convalescent he was always anxious as to the condition of his relatives or friends about him.

The typhus odor, usually likened to that of mice, was not pronounced in these cases. This may have been due to the bathing and constant care given to the patients by Dr. Percival, as well as to the very efficient system of ventilation insisted on in all the wards. On only one visit, when some new patients had just been brought into the ward, was the odor recognized. It was, as described, very offensive and sickening in character. All the nurses and orderlies, who of course see the typhus patients before they are washed, insist that the odor is always present and is very characteristic, especially on the first three days of the disease. If this is the case, it is a valuable symptom at a time when the fever is most difficult to recognize.

The cardinal symptom of typhus fever is, of course, the eruption. Until this appears, the diagnosis must remain uncertain. When it is abundant and well-marked, especially if petechial in character, there is generally no further room for doubt. An eruption of some sort was present in all of the cases under observation on North Brother Island, but it was not very characteristic as a

rule. It was usually dark-colored, but often very faint, the spots disappearing on pressure. In fact, many of these cases, if seen singly in their own houses, and without a history of exposure to contagion, would probably go unrecognized. Petechiæ were very rare, but present and persistent after death in most of the fatal cases.

Many of the above symptoms are to be noted only when the disease has been under observation for a certain length of time. Even when the principal ones are present, including the eruption, the diagnosis must sometimes be doubtful in the absence of a history. Dr. A. R. Mott¹ cites a case in illustration of this: A man was brought into Bellevue Hospital from the street, unconscious, and supposed to be drunk. The surface of the body was of a dusky hue, the face flushed, the eyes injected, and the pupils small. Over the abdomen and chest, and upper parts of the arms and thighs, were scattered, rather profusely, small petechial spots, mostly of minute size. The temperature was 40° C., the pulse 120, the respiration 36. Dr. E. G. Janeway saw the patient, and, while agreeing that the case was probably one of typhus, he saw nothing in the conditions that might not be as well explained—in the absence of previous history—by the presence of acute ulcerative endocarditis. The patient lived for thirty-six hours, and died without recovering consciousness. On autopsy, well-marked ulcerative endocarditis was found, with embolism of the middle cerebral and other smaller arteries of the brain, and infarcts in various organs. The spleen was normal in size and consistency.

There are other diseases, more common than ulcerative endocarditis, which may closely simulate typhus fever in many, if not all, of its symptoms. Such are, more especially, typhoid fever, measles, meningitis, acute lobar pneumonia, and uræmic coma. The history and course of the disease, with attention to the physical signs, are usually sufficient to enable a diagnosis to be made.

Of the one hundred and eighty-five cases on North Brother Island twenty-eight died, giving a mortality of fifteen per cent., which is rather less than the usual rate. Some of the deaths were due to complications, but the majority to the fever itself. Four autopsies were made, and all the organs examined except the brain and spinal cord. The pathological appearances were pretty nearly the same in all, varying only in degree. These lesions were—acute degeneration in the liver and kidney, with swelling and hyperplasia of the spleen. The other viscera presented no noteworthy changes.

¹ American Journal of the Medical Sciences, April, 1884.

In the liver there was a moderate degree of swelling and increased granulation of the liver-cells. Careful search was made for such minute foci of cell-necrosis as have recently been described as present in several acute infectious diseases, but with negative result. In one case, which died while the temperature was very high, I noticed, in a degree which is very unusual, an accumulation of large, irregular, moderately granular cells, either free in the liver capillaries or clinging to their walls. These cells appeared to be swollen and detached endothelium. A typical portion of this liver is represented in Fig. 1.

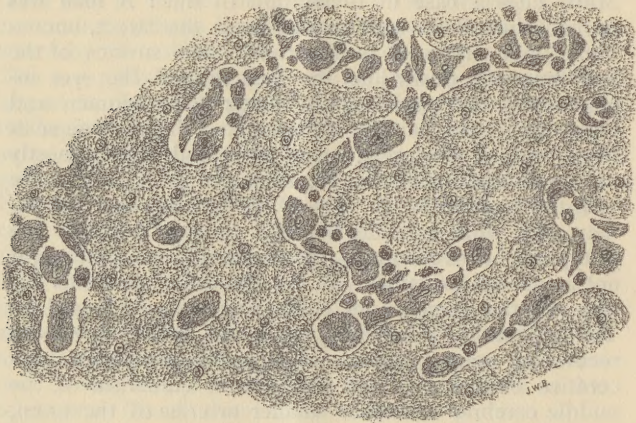


FIG. 1.—Section of Liver, showing Cells in the Capillaries.

I would not attach especial significance to this lesion of the capillaries in connection with this disease, but simply record it as a contribution to the too little understood lesions of vascular endothelium in acute infectious diseases.

The kidneys showed granular degeneration of the tubular epithelium, with considerable disintegration. The spleen presented the usual appearances of acute hyperplasia.

J. W. B.

THE most important studies hitherto made on the etiology of typhus fever are those of Hlava, of Thoinot and Calmette, and of Lewaschew.

Studies of Hlava.¹—In 1888 Hlava, during an epidemic of typhus fever in Prague, examined bacteriologically the blood and viscera of thirty-three cadavers, and the blood-crysts and urine of ten cases during life. A bacillus was isolated from the blood of twenty of the cases which had died, and from two of the living patients. This bacillus differed from any known form. He described it as an "ovoid coccus," or a very short bacillus, growing in pairs and in chains. From this latter growth-character he termed it a "strepto-bacillus." Its diameter varied from $0.9\ \mu$ to $1.2\ \mu$, the length of the ovoids was about $0.9\ \mu$, that of the bacilli $1.8\ \mu$, while the terminal individuals of the chains grew to the length of 2 to $3\ \mu$. In broth it developed rapidly at body temperature, forming chains, and was without visible spores. No growth was obtained in gelatine at 20°C .

Plated in agar, the deep colonies were circular or oval, and opaque, the surface colonies circular, lace-like, and whitish, with an opaque centre and transparent edges. The diameter of the largest colonies did not exceed 2 mm., and when magnified about one hundred diameters they appeared granular and showed very fine threads on their borders. The growth on human blood-serum presented the same characters. No growth was found on potato. Human and veal broth showed a rapid growth, which settled in the form of a white precipitate, while the fluid above remained clear. The "strepto-bacilli" died in eight days in broth, and in twelve to fourteen days in agar. They stained with all the aniline dyes and by Gram's method.

Culture inoculations of the strepto-bacillus in rabbits, guinea-pigs, dogs, cats, mice, and pigeons were not fatal; a slight elevation of temperature was noted for a few days, after which they recovered. The animals were killed and platings made from the organs, but the inoculated bacillus was not found.

Inoculations in two young pigs gave more positive symptoms. In one case the temperature rose to 41.4°C . on the eighth day, and for sixteen days remained above 39°C . On the fifth day small reddish spots appeared on the skin, and disappeared after three days. In the other case no spots appeared.

Loss of appetite and flesh were marked symptoms in both cases. The animals were killed, and on autopsy

¹ Hlava: Archives Bohême de Médecine, 1889-90, vol. iii., p. 122 (Sborink Lékárský).

showed a "degeneration" of the kidneys and tumefaction of the spleen. The bacilli were not found in the blood or spleen, but were found in the kidneys of one case, and in an area of broncho-pneumonia in the injected lung of the other. Virulence of the cultures for young pigs was lost after a short time.

Thus, in brief, Hlava found the "strepto-bacillus" in the cadavers of twenty out of thirty-three cases which had died of typhus fever, and in two out of ten cases, from the blood during life. The results of his animal experiments seem to be of little significance.

Studies of Thoinot and Calmette.¹—These writers studied seven cases of typhus fever during an epidemic of the disease on the island of Tudy. Platings were made from the blood of all the cases and gave negative results. Inoculations of blood were made in rabbits, guinea-pigs, and pigeons, with negative results. The only positive results obtained were from the examination of fresh unstained blood, and in this these observers found constantly present, certain motile "granules," measuring 1 to 2 μ , provided usually with a short, thread like prolongation. Unattached motile threads were also found. These bodies moved rapidly among the blood cells. The writers claim that this "organism" differs from forms of degenerated blood-cells described by various writers.

Studies of Lewaschew.²—Lewaschew found constantly in fresh blood from the spleen in "numerous cases"—he does not state how many—minute organisms, sometimes appearing as threads, sometimes as spheres having a thread-like attachment, which move actively among the blood-cells. He also obtained from spleen puncture and finger-blood a slow-growing micrococcus which he has not yet described, nor does he state the number of cases in which he found it.

Original Studies.—The primary purpose of this paper is to record the results of a morphological and biological study, made during the recent outbreak of typhus fever in New York City, with a view of throwing some light, if possible, on the etiology of the disease.

The material was furnished to me by Dr. Brannan, and consisted of the viscera from three cadavers, and blood obtained by finger-puncture from six living patients during the height of the disease, while the temperature recorded was 40° C. or over.

Examination of the Viscera.—These were brought to the laboratory uncut, wrapped in cloths moistened in one

¹ Annales de l'Institut Pasteur, tome vi., No. 1, January, 1892.

² Deutsche Med. Wochenschr., Bd. 18, No. 13, p. 279, 1892.

pro mille bichloride solution, and platings and sowings were made at once on their arrival, with the usual precautions against contamination. Portions were hardened in alcohol for morphological study.

CASE I.—Sections¹ of the spleen and kidney were stained by Gram's method, and examined under a one-sixteenth oil immersion, for any micro organism which might be present, but none were found.

Platings were made on six per cent. glycerine, agar, and sowings in beef broth, from the heart's-blood, spleen, and kidney, and kept at 37.5° C. and at room temperature. The plates were kept under observation for twelve days, and the tubes for a much longer period, but no growth occurred.

CASE II.—Sections of the spleen and kidney were stained and examined as in the former case, with a like negative result.

Cultures were made as in Case I., but only a negative result was obtained after twelve days of observation.

CASE III.—In sections of the spleen, liver, and kidney no micro-organisms of any kind were found.

Cultures were made from the heart's-blood, spleen, kidney, and liver. The platings were on beef blood-serum, and on six per cent. glycerine agar, in Petri dishes, and in Blücher's anaerobic plates. The sowings were in beef blood-serum, both fluid and coagulated, in sealed and unsealed tubes; in beef broth and glycerine agar tubes; by deep puncture in alkaline agar tubes, and in Nikiforoff's anaerobic tubes, charged with six per cent. glycerine beef broth. All of these cultures were kept at 37.5° C., and were studied daily for sixteen days, many of the tubes for a much longer period. In no case was there any growth, except some scattering later contaminations on the plates.

Examinations of the Blood.—The blood, obtained under strict antiseptic precautions from the six living patients, was streaked on six per cent. glycerine agar plates, and smeared on sterilized cover-glasses by Dr. Brannan, and brought at once to the laboratory. The cover-glass blood-smears from all the cases being dried at once in the air, were fixed in alcohol, and stained in Czenzynski's solution for eighteen hours, at room temperature. Although all of these covers were examined throughout with a one-sixteenth homogeneous immersion lens in the most careful manner, in only about one-half of them a few blue-stained bacilli were found, never more than eight or ten on a cover.

¹ These sections were examined by me only for micro-organisms; the histological examinations are described above by Dr. Brannan.

In length they never exceeded one-third of the diameter of a red blood-cell, although usually not more than half that length. The diameter was not more than half the length of the smaller bacilli. They were round-ended, and were usually found singly, lying apart from the blood-cells, but in a few instances groups of from three to six bacilli were seen.

Platings, made from the blood of the six patients, were kept at 37.5° C., and showed a growth of colonies among the blood-cells in from two to four days. In all of the cases some of the plates remained sterile, while the plates on which growth was found developed a very variable number of colonies. In one case between sixty and seventy colonies developed on one plate, in another case twenty-six were found, while but one single colony was developed on each of two plates in one of the cases examined. These colonies, while thus present in varying numbers in all of the six cases, presented the same general appearance. Cover-glass preparations showed that the colonies were formed of small bacilli, and subsequent morphological and biological study has proved them to be identical in all the different cases.

Description of the Bacillus.—*Morphology.*—The diameter of the bacillus varies from $0.5\ \mu$ to $0.8\ \mu$, and the length from $1.0\ \mu$ to $2.5\ \mu$. It occurs singly and in pairs (Fig. 2),



FIG. 2.—Bacilli from Culture, showing Irregularities of Form and Staining.

infrequently in short chains of six or eight. It is often club shaped, and is found to be ovoidal in young cultures. It stains readily with the ordinary aniline dyes, and retains the color after staining by Gram's method. After some days' growth certain of the bacilli stain irregularly, presenting a sort of mottled appearance. The bacilli are immobile, and spores were not found, although some of the club-shaped bacilli show circular unstained spots which do not color by the methods usually employed for spore-staining.

Mode of Growth.—Under the most favorable circum-

stances growth is not voluminous. The most abundant growth obtained was on beef blood-serum at 37.5° C. No growth was obtained on gelatine, nor on any medium at a temperature under 27° C. Development occurs under mica plate, and in an atmosphere of hydrogen, but the growth is not so abundant as in aerobic cultures.

The colonies of this bacillus growing on six per cent. glycerine agar plates present to the naked eye, in about eighteen hours, in oblique light, a scanty growth, consisting of minute, bluish gray, translucent spots. The diameter of the largest colonies at this time does not exceed 0.25 mm. Older colonies appear dry and scaly to the naked eye, are flat, whiter, and more opaque, and never exceed 2 mm. in diameter. These colonies, when examined by a hand magnifying-glass, show a central thickening. The younger colonies, examined under low powers, are rounded in outline, the surface is granular, the edge sinuous and sharply defined. On very moist agar the sharp definition of the edge is lost. Under these low powers the colony has a pale brown color, which is deeper in the centre and in scattered points over the surface, an appearance probably due to the irregular heaping of the growth. When magnified about one hundred diameters the surface appears coarsely granular, and the edge is formed of short, coarse, irregular spiculæ.

Glycerine agar tubes at 37.5° C. show the same surface-growth appearances as the plates. In the line of puncture small, white, isolated colonies occur, and in the condensation water there is a white deposit, quite perceptible in twenty-four hours, the fluid above remaining clear.

On coagulated beef blood-serum, at 37.5° C., the growth is slightly elevated, white, and shiny. In beef broth at 37.5° C. the growth is slight, and settles in the form of a white precipitate, the fluid above remaining clear. In milk at 37.5° C. growth occurs in the form of a white deposit—the milk undergoes no apparent change. No visible growth was obtained on potato or on macaroni.

Animal Experiments.—Inoculations of from $\frac{1}{4}$ to $\frac{1}{2}$ c.c. of a broth culture from patient J. S.— were made in the ear-vein of two rabbits, and in the subcutaneous tissue of the abdomen of one rabbit and two guinea-pigs, and in two white mice.

All the animals lost flesh rapidly. The two guinea-pigs died on the tenth day, on the twelfth day one mouse and one rabbit died, and on the thirteenth day the remaining mouse died, and the two remaining rabbits were killed. Examinations of all these animals, made

as early as practicable after death, showed nothing abnormal in the gross appearance of the viscera. Cultures were made from the blood and viscera of the guinea-pigs, and from the heart's-blood of all the other animals, but the inoculated bacillus was found only in the case of the rabbit which died on the twelfth day after inoculation in the ear-vein.

Another series of inoculations were then made in the ear-vein of five rabbits, of about $\frac{1}{2}$ c.c. each, of a seven-day broth culture from patient M—. The animals all showed marked emaciation, and all of them died, one each on the nineteenth, twenty-first, twenty-third, twenty-fourth, and twenty-ninth days. The heart's-blood of these animals was plated, and the inoculated bacillus recovered only from one set of plates, those made from the rabbit that died on the twenty-first day.

Summary of Inoculation Experiments.—Inoculations of cultures of the bacillus obtained from two of the cases were made in eight rabbits, two guinea-pigs, and two white mice. All the animals showed marked emaciation, and with the exception of two rabbits all the animals experimented upon died in from ten to twenty-nine days. The inoculated bacillus was recovered from the heart's-blood of two of the rabbits that died.

Remarks.—The bacillus found seems to be a species hitherto undescribed. Biologically it bears considerable resemblance to the "strepto-bacillus" of Hlava—morphologically it differs, being somewhat smaller and there being but the slightest tendency to the formation of chains, which in the case of the bacillus of Hlava is described as a marked character. A striking difference is also shown in the effect of its inoculation in animals.

All things considered, the writer cannot believe this bacillus—for which the name *Bacillus sanguinis typhi* is suggested—to be identical with the "strepto-bacillus" described by Hlava.

General Summary.—Morphological and biological examination of the blood and viscera of three patients, dead of typhus fever, gave a negative result.

Morphological and biological examination of finger-blood from six living patients showed in every case the presence of a bacillus in very small numbers. This bacillus is pathogenic for rabbits, guinea-pigs, and white mice, but though pathogenic in these animals the effect which it produces upon them is not one contributing material evidence in favor of its etiological relationship to typhus fever. Indeed this is what might be expected, since, so far as we know, these animals are not subject to the disease. The fact of finding a new species of bacillus

in the blood of six consecutive patients, with uncomplicated typhus fever, in the height of the disease, seems significant, and is suggestive of an etiological relationship of the bacillus found to the disease.

This relationship cannot be determined by a single limited research. The proof must be furnished by an accumulation of evidence, either along lines such as have been pursued in this investigation, or in directions which may present themselves as our knowledge increases.

T. M. C.

